

D0017 NP

Claims 12 and 23 were objected to because those claims referred to method claims but did not depend from method claims. This objection is obviated by the amendment of claims 12 and 23 to depend from claims 11 and 22, respectively. Withdrawal of the objection to claims 12 and 23 is respectfully requested

### III. Rejection under 35 U.S.C. §112, first paragraph

Claims 1-23 were rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection. Nevertheless, the rejection of claims 1-23 under 35 U.S.C. §112, first paragraph is obviated by the amendment of claims 1 and 13 to delete the term "high volume". Claims 1 and 13 have been amended to recite vectors for use in a high throughput anti-viral assay. Claims 11 and 22 have been amended to recite high throughput methods of screening for compounds. Support for these amendments can be found in the application as originally filed. For example, support for the amendments can be found at page 1, line 26, page 4, lines 27-30 and page 9, lines 4-8. Thus, withdrawal of the rejection of claims 1-23 under 35 U.S.C. §112, first paragraph is respectfully requested.

### IV. Section 102 Rejections

Claims 1, 4, and 10 were rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. The basis for this rejection is that claims 1, 4 and 10 are directed to replication competent HIV-1 viral vectors in which a non-essential region for viral replication has been replaced by a reporter gene. Applicants respectfully traverse this rejection.

Applicants respectfully submit that the claims as amended are not anticipated by Chen. The claimed invention is directed to vectors for use in a high throughput anti-viral assay wherein the vector encodes a replication competent HIV-1 virus, the vector comprising an HIV-genome in which a region non-essential for viral replication has been replaced by a reporter gene that serves as a marker for viral replication and can be analyzed in a simple and rapid manner.

Previous attempts to modify HIV-1 proviral clones with a reporter gene failed to produce replication competent reporter viruses useful in high throughput assays. For example, as set forth in the present

D0017 NP

specification, the JRFNFLuc virus, which encodes a firefly luciferase gene, was constructed in a manner similar to that set forth in Chen. As set forth at page 17 of the present specification, this virus failed to produce firefly luciferase after the third day of infection, indicating that mature virus core particles were not made and that the virus was not replication competent. Accordingly, at the time of the present invention, the art failed to teach or suggest the replication competent reporter viruses of the present invention which are useful in high throughput assays.

Chen does not disclose or suggest the claimed invention. Withdrawal of the rejection of claims 1, 4 and 10 under 35 U.S.C. §102(b) as anticipated by Chen is respectfully requested.

The Examiner has rejected claims 1, 4, 10 and 11 under 35 U.S.C. 102(b) as being anticipated by Haseltine. This rejection is respectfully traversed. The Office Action states that Haseltine "teaches a replication competent HIV-1 virus with a deletion in a non-essential region of the virus" and "a reporter gene to trace HIV replication or monitor the effects of anti-HIV drugs in a screening assay." Applicants respectfully traverse this rejection.

It is well-established that anticipation requires the disclosure in a single prior art reference of each element of the claim. Applicants respectfully submit that the claims as amended are not anticipated by Haseltine. Claims 1, 4 and 10 are directed to vectors for use in high throughput anti-viral assays wherein the vector encodes a replication competent HIV-1 virus, the vector comprising an HIV-genome in which a region non-essential for viral replication has been replaced by a reporter gene that serves as a marker for viral replication and can be measured in a high throughput assay anti-viral assay. Claim 11 is directed to a high throughput method of screening for compounds that exhibit anti-viral activity against HIV-1 utilizing a vector of claims 1, 2 or 3.

As discussed in the Background of the Invention section of the present specification (pages 2-3), single-cycle infectious HIV-1 reporter viruses encoding luciferase as the reporter gene have been described, but steps post-HIV gene expression in an infected cell, such as HIV protease mediated processing of viral precursor polypeptides required for virion maturation, are not easily measured using such reporter viruses. Thus, such viruses are not useful for testing for possible late stage replication inhibitors. Also, replication-

D0017 NP

competent HIV-1 reporter viruses are known, but are not useful for high throughput anti-viral assays because the reporter gene products they encode cannot be measured by simple and rapid assays. Haseltine discloses an example of such a virus.

The claims as amended are directed to vectors for use in high throughput anti-viral assays. Haseltine merely discloses a replication competent HIV-1 reporter assay encoding CAT, which, as stated above, is not useful in high volume anti-viral assays.

Haseltine does not disclose or suggest the claimed invention. Accordingly, withdrawal of the rejection of claims 1, 4, 10 and 11 under 35 U.S.C. §102(b) as anticipated by Haseltine is respectfully requested.

**V. Section 103 Rejections**

Claims 1, 5-9 and 15-21 were rejected under 35 U.S.C. 103(a) as being unpatentable over Chen as applied to claims 1, 4 and 10 and further in view of Gibbs, Shi, Collman or Li. This rejection is respectfully traversed.

Applicants respectfully submit that the claims as amended are not obvious over Chen and further in view of Gibbs, Shi, Collman or Li. As discussed above, the Chen reference does not disclose or suggest Applicants claimed replication competent HIV-1 viral vector in which a region non-essential for viral replication has been replaced by a reporter gene wherein expression of the reporter gene is dependent on replication of the HIV-1 virus and the expression of the reporter gene can be measured in a high throughput anti-viral assay

The Gibbs, Shi, Collman and Li references do not remedy the deficiencies of Chen.

Accordingly, withdrawal of the rejection of claims 1, 5-9 and 15-21 under 35 U.S.C. §103(a) as obvious over Chen in view of Gibbs, Shi, Collman or Li is respectfully requested.

The Examiner has rejected claims 1-3, 11-14, 22 and 23 under 35 U.S.C. 103(a) as being unpatentable over Chen, Haseltine and Liu. Applicants respectfully traverse this rejection.

D0017 NP

Applicants respectfully submit that the claims as amended are not obvious over Chen, Haseltine and Liu. As discussed above, Chen and Haseltine alone or in combination do not disclose or suggest Applicants claimed invention. Furthermore, Liu does not cure the deficiencies of the Chen and Haseltine references. The viral vector described in Haseltine is not suitable for use in a high throughput screening assay due to the limitations of the reporter used. Haseltine does not suggest any manner of remedying these problems and does not describe how one skilled in the art would modify the HIV-1 virus of Haseltine to arrive at the present invention. Merely pointing out that a reporter used in the present invention was known in the art, as the Examiner has done by citing Lui, does not remedy this deficiency. Moreover, as stated above, Chen is an example of a luciferase reporter which failed to result in a replication competent HIV-1 virus. As such, this is evidence that merely suggesting that a particular luciferase reporter may be used in a HIV-1 virus does not provide the necessary teaching to arrive at the present invention.

For the reasons discussed herein, Applicants submit that the claims as amended are not obvious over Chen, Haseltine and Liu. Accordingly, withdrawal of the rejection of claims 1-3, 11-14, 22 and 23 under 35 U.S.C. §103(a) as being unpatentable over Chen, Haseltine and Liu is respectfully requested.

#### VI. Conclusion

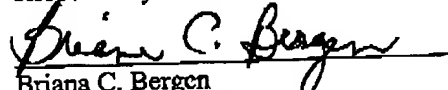
Applicants respectfully submit that the claims are in condition for allowance. Please direct any questions concerning this Response or any aspect of this case to the undersigned attorney.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

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Date: September 28, 2005

Respectfully submitted,

  
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